

U.S. and States Ramp Up Response to Opioid Crisis

Regulatory, Legislative, and Legal Tools Brought to Bear

Stephen Barlas

Opioid addiction has vaulted onto the front pages of the nation's newspapers and to the top of Washington's political agenda. Politicians in both parties and at all levels of government have raised what many call a "crisis" to a level of public attention it has never seen before. In mid-July, the *Washington Post* started a front-page story by citing 96 fatal overdoses in the first four months of 2017 in Cincinnati and quoted the city's coroner saying the opioid epidemic ravaging western Ohio and scores of other communities along the Appalachian Mountains and the rivers that flow from it continues to worsen.¹ Less than one week later, the *Post* ran another front-page story entitled, "A 10-Year-Old's Overdose Death Reveals Miami Neighborhood's Intense Struggle With Opioids."²

"Opioid addiction and the resulting overdoses and deaths ... [are] in my view, the toughest public health challenge that we face at FDA," said Scott Gottlieb, MD, Commissioner of the Food and Drug Administration (FDA), who in July announced new requirements for risk evaluation and mitigation strategy (REMS) programs for opioids, including new training requirements for pharmacists.³

Concern from Republican senators about reductions in Medicaid spending on addiction services partially accounted for the demise of the Senate's Patient Protection and Affordable Care Act (PPACA) "repeal and replace" bill in July. In June, the Justice Department announced the largest-ever health care fraud enforcement action by arresting more than 400 doctors, nurses, and other health care professionals for false billing for opioid prescriptions.⁴

States have been just as active. Multiple lawsuits alleging illegal support of opioid distribution have been filed by state attorneys general. Many of those states are trying to beef up their prescription drug monitoring programs (PDMPs), which have traditionally been weak in many places, and to find ways to provide naloxone to Medicaid recipients while keeping Medicaid budgets from exploding.

Soaring rates of deaths from abuse of primarily immediate-release opioid products, such as oxycodone (OxyContin, Purdue Pharma), hydrocodone (Vicodin, AbbVie), morphine, and methadone, have captured Washington's imagination in a way they never did during the Obama administration. And the rise of opioid addiction as a front-line political issue has far surpassed other pharmaceutical concerns—such as the bemoaned but politically ignored price of prescription drugs.

Addiction is heavily weighted toward rural areas, such as those along the Appalachians highlighted by the Cincinnati

coroner. The *Washington Post* story highlighting Miami acknowledged: "Opioids are best known as a scourge of white, working-class America from the Midwest to New England, but the nation's big cities, too, have been increasingly brutalized."² There is undoubtedly abuse in Beverly Hills and on Wall Street. But stories in the press consistently feature abusers in middle-American, rural locales such as Oklahoma, Alabama, and Ohio.

Opioids—prescription and illicit—are the main driver of drug overdose deaths. Opioids were involved in 33,091 deaths in 2015, according to the Centers for Disease Control and Prevention (CDC), and opioid overdoses have quadrupled since 1999.

In 2015, the five states with the highest rates of death due to drug overdose were West Virginia (41.5 per 100,000), New Hampshire (34.3 per 100,000), Kentucky (29.9 per 100,000), Ohio (29.9 per 100,000), and Rhode Island (28.2 per 100,000). Deaths associated with the most commonly prescribed opioids rose 9.1% in the Northeast and 4.8% in the South between 2014 and 2015, while deaths blamed on synthetic opioids other than methadone, such as fentanyl, skyrocketed 107.4% in the Northeast and 95.0% in the Midwest.⁵

The Problem in Brief

Over the past decade, prescription opioids for pain have been the issue, mostly immediate-action drugs prescribed by physicians, but sometimes longer-lasting versions, too. Excessive prescription, especially to patients who ought to have been weaned off the drugs—such as someone with acute back pain or a toothache as opposed to a cancer patient—has led to addiction to opioids, and also led many to heroin, which is cheaper and easier to obtain. State attorneys general have sued drug stores and drug distributors recently for supplying "pill mills" and other perceived crimes.

In the last couple of years, physicians have appeared to become stingier with opioid prescriptions. The CDC reported in June that the number of prescriptions for opioids such as oxycodone written by health care providers between 2012 and 2015 dropped 13.1% over the three-year period, from 81.2 per 100 people to 70.6. The *Washington Post* quoted Anne Schuchat, MD, the CDC's Acting Director at the time: "It looks a little bit better, but you really have to put that in context. We're still seeing too many people get too much for too long." Dr. Schuchat said in the interview that the prescription rate is still triple the level it was in 1999 and four times what it is in some European countries.⁶

But the drugs responsible for what some call a "crisis" have begun to morph a little as deaths from overdoses of fentanyl have risen rapidly, not as a result of prescription abuse, but from nonprescription fentanyl mixed with or



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U.S. and States Ramp Up Response to Opioid Crisis

substituted for heroin or other illicit substances. In July, a House Energy and Commerce subcommittee held a hearing entitled “Combating the Opioid Crisis: Battles in the States” during which John Tilley, Secretary of the Justice and Public Safety Cabinet for the State of Kentucky, said the percentage of overdose deaths from drugs attributed to fentanyl rose from 34% in 2015 to 47% in 2016. Kentucky State Police reported a 6,000% increase in laboratory samples submitted to the Central Forensic Laboratory testing positive for fentanyl from 2010 to 2016. Last year, in addition to fentanyl, the Kentucky State Police reported samples from 10 different counties testing positive for carfentanil, a fentanyl analogue, which is 100 times more potent than fentanyl itself.⁷

According to U.S. law enforcement and drug investigators, China is the primary source of deadly fentanyl in the United States. “It appears most of the fentanyl produced in China is intended for export to our communities,” U.S. Senator Rob Portman (R-Ohio) said at a Senate hearing about U.S. strategy to combat illicit drugs. The majority of the packages arrive here via the U.S. Postal Service (USPS), which Senator Portman blames for not providing enough information, and no electronic information, to the Customs and Border Protection (CBP) agency, which is responsible for identifying suspect packages and inspecting them. The USPS and the CBP have one pilot program at one of five USPS intake centers at JFK airport in New York where the USPS is providing advanced electronic data to CBP for packages that weigh less than 4.4 pounds (known as “ePackets”). Once the USPS shares the information, CBP uses it to identify the packages it wants to inspect. The USPS then locates and presents those selected packages for inspection. “While this is a step in the right direction—after nearly 15 years of inaction—the results to date are lacking,” Senator Portman argued. “At the other four centers (JFK is the fifth), the Postal Service is stuck sifting through millions of packages trying to find a needle in a haystack. We can’t continue like this. We need more advanced electronic data, and we need it now.”⁸

The Federal Response

The rise of fentanyl and carfentanil had not yet occurred when President Barack Obama announced his Prescription Drug Abuse Prevention Plan in 2010. That plan raised the profile of opioid abuse ever so slightly, but the Obama administration did very little of value until the end of the president’s term. The Department of Health and Human Services (HHS) waited until 2015 to unveil its Opioid Initiative. One Washington representative of an addiction advocacy group says, “We were constantly barking at them to do something.” He does credit the administration for initiating a new grant program at the HHS for medication-assisted treatment (MAT), which began in 2015 with 11 states receiving a total of \$12 million. More states were added in fiscal 2016 and 2017; the 2017 pot is \$26 million, and five new states will be added.⁹ Certainly passage of the PPACA helped, too. It made substance abuse treatment one of 10 required areas of coverage for marketplace plans, and the law also expanded Medicaid coverage for able-bodied individuals under certain income limits; that coverage can be applied to substance abuse treatment.

At the very end of President Obama’s tenure in 2016, Congress passed the 21st Century Cures Act, which allocated

\$1 billion over two years to enhance states’ response to the epidemic. The Cures Act set up a new grant program within the HHS called the State Targeted Response (STR) to the Opioid Crisis Grants. A little less than \$500 million in new money in both fiscal 2017 and fiscal 2018, over and above \$53 million in opioid grants from HHS in fiscal 2016, will be distributed to all states and territories based on the degree of their opioid addiction problem. The grants will provide support to states for increasing access to treatment, reducing unmet treatment need, and reducing opioid-related overdose deaths.¹⁰

Robert Morrison, Executive Director and Director of Legislative Affairs for the National Association of State Alcohol and Drug Abuse Directors, says states have some freedom with how they use the funds, although 80% of the grants have to be devoted to treatment and recovery programs, 5% to administration, and the remaining 15% to what the state sees fit, including prevention. “The STR grants are very big and represent about a 10% increase in state addiction treatment budgets, on average,” Morrison explains. But the \$500 million pales against the \$10 billion Medicaid will spend on addiction programs in 2017.

It is unclear how big a dent in the untreated population those new grants will make. Mark Dunn, Director of Public Policy for the National Association of Addiction Treatment Providers, says there are an insufficient number of treatment beds for opioid addicts. Dennis Fisher, PhD, and colleagues from California State University at Long Beach, published an analysis in the February 2017 edition of the *Journal of Substance Abuse Treatment* that examined the discrepancy in the number of people who access substance abuse treatment and the number who need treatment, with that gap being “sizeable.”¹¹ “In our paper, we showed that the number-one reason for failing to get into treatment was no room in the drug treatment program that they applied to,” Dr. Fisher explains.

Of course, it makes sense to limit the need for treatment by limiting the availability of opioids in some situations. In June, the FDA requested that Endo Pharmaceuticals remove its opioid pain medication, reformulated Opana ER (oxymorphone hydrochloride), from the market. The agency reasoned that the benefits of the drug might no longer outweigh its risks. While Endo defended “the safety, efficacy, and favorable benefit-risk profile of Opana ER when used as intended,” it agreed to voluntarily remove it from the market.

That was the first time the FDA has taken steps to remove a currently marketed opioid pain medication from sale due to the public health consequences of abuse. Then, weeks later, Commissioner Gottlieb announced that the agency intends to update the existing REMS programs on extended-release opioid analgesics, and for the first time extend these same regulatory requirements to the manufacturers of immediate-release opioid analgesic products. The emphasis will be on making sure providers understand the current thinking on the dosing of the products. In addition to training for physician prescribers, the REMS will require that training also be made available to other health care providers involved in the management of patients with pain, including nurses and pharmacists.³

Attorney General Jeff Sessions has been very active, too. In addition to the June announcement of the biggest-ever health care fraud case related to bogus opioid prescriptions, the Justice

U.S. and States Ramp Up Response to Opioid Crisis

Department revealed one month later that it had reached a \$35 million settlement with Mallinckrodt Pharmaceuticals to resolve allegations that the company failed to report signs that large quantities of its highly addictive oxycodone pills were diverted to the black market in Florida. The Justice Department said the deal establishes “groundbreaking” new standards that require the company to track its drugs as they flow through the supply chain to consumers in an effort to control the epidemic.¹²

Struggles at the State Level

The fact that the new 21st Century Cures STR grants to the states require a heavy emphasis on treatment means that many states will be able to upgrade MAT programs. Terry Horton, MD, Chief of the Division of Addiction Medicine and Associate Physician Lead of the Behavioral Health Service Line at Christiana Care Health System in Wilmington, Delaware, says, “Several decades of medical research has taught us that effective opioid drug treatment requires a long-term approach with medication-assisted therapies, such as methadone and buprenorphine, counseling support, and similar means to assist with psychosocial challenges. Compared to counseling alone, participation in MAT resulted in approximately a 50% reduction in overdose fatalities.” Dr. Horton adds that Delaware’s largest substance use disorder treatment provider first began MAT when Medicaid began to cover the cost of that care. It now provides thousands of outpatient treatment slots for patients with opioid addiction—slots that he explains were at risk of being eliminated under the House and Senate PPACA repeal proposals because of the potential elimination of the PPACA’s Medicaid expansion and cuts to pre-expansion Medicaid programs.

To be able to prescribe buprenorphine, physicians must take and pass a test. Initially, they were allowed to treat only 100 patients, a cap that was increased last year to 250. Some physicians are able to join the program without taking the test via a waiver process. All three FDA-approved opioid treatment medications (methadone, buprenorphine, and naltrexone) are covered under the Medicaid Drug Rebate Program. The associated copays and authorization requirements vary from state to state. However, Morrison explains that it is one thing for a physician to be qualified to prescribe buprenorphine; it is another for them to actually do so. Many don’t for reasons having to do with insufficiency of Medicaid reimbursement or simply not wanting to treat that “particular patient” population. Other physicians won’t buy into the notion of treating drug addiction with drugs, Morrison states.

MAT programs in the states vary widely, as do PDMPs—state-run electronic databases of prescriptions for controlled substances. PDMPs can provide a prescriber or pharmacist with information regarding a patient’s prescription history, allowing prescribers to identify patients who are potentially abusing medications. With Missouri adopting a PDMP in April 2017, all 50 states, the District of Columbia, and Guam have legislation authorizing the creation and operation of a PDMP, and all but the District of Columbia program are operational. The House Energy and Commerce Committee staff, in preparation for a July 2017 hearing the committee held on state responses to opioid addiction, prepared a background memorandum

that said, “While there is evidence indicating the potential of PDMPs to identify high-risk patients and impact prescribing behaviors, the effectiveness of PDMPs is constrained by the lack of consistent utilization, timely data in some states, and limited interoperability with other PDMPs.” CDC experts have found that a few states have been able to change prescribing patterns by increasing prescriber use of their PDMPs. New York and Tennessee, for example, mandated prescriber use of the state PDMP in 2012. They subsequently used their PDMPs to document declines of 75% and 36%, respectively, in their inappropriate use of multiple prescribers by patients.

The Missouri program underscores the difficulty of turning PDMPs into potent anti-abuse weapons. Missouri’s governor, Eric Greitens, signed an executive order in mid-July requiring pharmacy benefit managers to forward data on prescriptions to the state health department. Only when the second phase of the program goes into effect will pharmacies be required to report opioid prescriptions to the state. Neither physicians nor pharmacies will have access to that data, and Missouri will not be establishing a “pill shopping” database as other states have.¹³

The fact that many PDMPs have shortcomings may be forcing state law enforcement agencies to take more aggressive steps to blunt the crisis. A more recent strategy at the state level has been to file lawsuits against drug manufacturers, distributors, and pharmacies. This summer, the attorneys general in Ohio, Missouri, and Oklahoma plus the district attorneys for three counties in Tennessee filed suits against the industry. The suits target some of the biggest names in the business, including McKesson, Johnson & Johnson, and CVS.

Ohio Attorney General Mike DeWine charged in his suit that 10 manufacturers didn’t tell consumers the truth about their products and that their marketing claims are not supported by science and medical evidence, a violation of the Food, Drug, and Cosmetic Act. In the lawsuit, which makes arguments mirroring those in similar recent suits, Ohio says that by the late 1990s (and continuing today) “each defendant began a marketing scheme designed to persuade doctors and patients that opioids can and should be used for chronic pain, a far broader group of patients much more likely to become addicted and suffer other adverse effects from the long-term use of opioids.” Defendants in the case include Purdue Pharma, Teva Pharmaceutical Industries, Johnson & Johnson, Endo Pharmaceuticals, and others.¹⁴

The companies argue they haven’t broken any laws and are doing what they can to pitch in against the opioid abuse tsunami. Purdue Pharma, for example, is funding a National Sheriffs’ Association program that delivers naloxone overdose kits and trains front-line officers. Naloxone is a “rescue drug” that can reverse an overdose from some opioids, including heroin. “Purdue remains committed to combatting opioid abuse and equipping our communities with the tools and resources they need to do so,” said Gail Cawkwell, Chief Medical Officer of Purdue Pharma.¹⁵

While the FDA is trying to take some products off the market, it is also trying to make Narcan (Adapt Pharma, Inc.), the inhaled form of naloxone, more readily available by allowing it to be sold over the counter, which would require the product to have a drug facts label. One does not exist at the moment, and the FDA is apparently working to fill that void. Currently,

continued on page 592

U.S. and States Ramp Up Response to Opioid Crisis

continued from page 571

the drug can only be obtained with a prescription, and the average wholesale price for a single dose is \$75.¹⁶ Local police departments, sheriffs' offices, and other personnel who are out on the street treating overdose victims say it isn't unusual for them to administer Narcan to the same person repeatedly over a period of time. At that rate, some agencies are rationing Narcan, and even if they weren't, one wonders how much of a solution to the crisis the drug really is.

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